

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

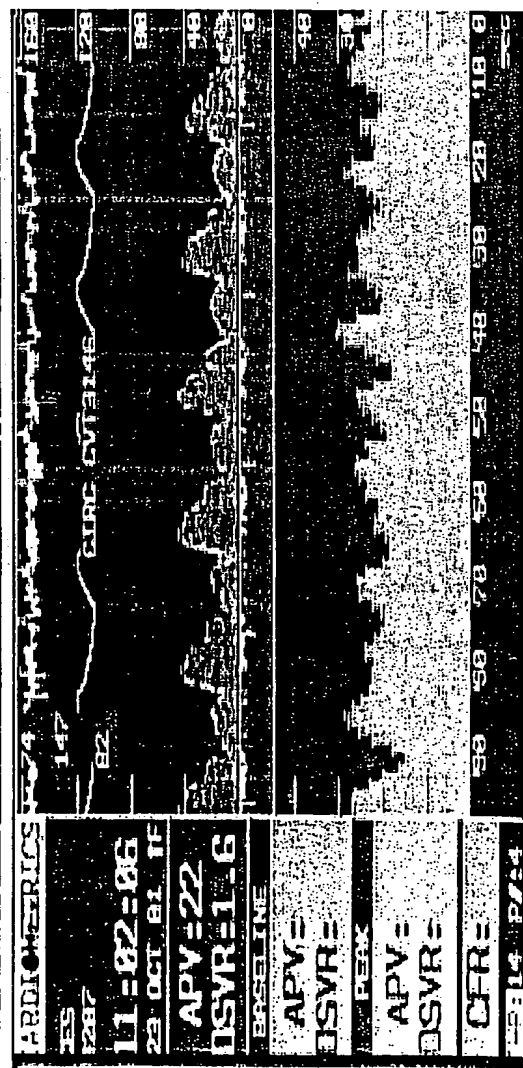
IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

Intracoronary Doppler Flow Velocity Profiles



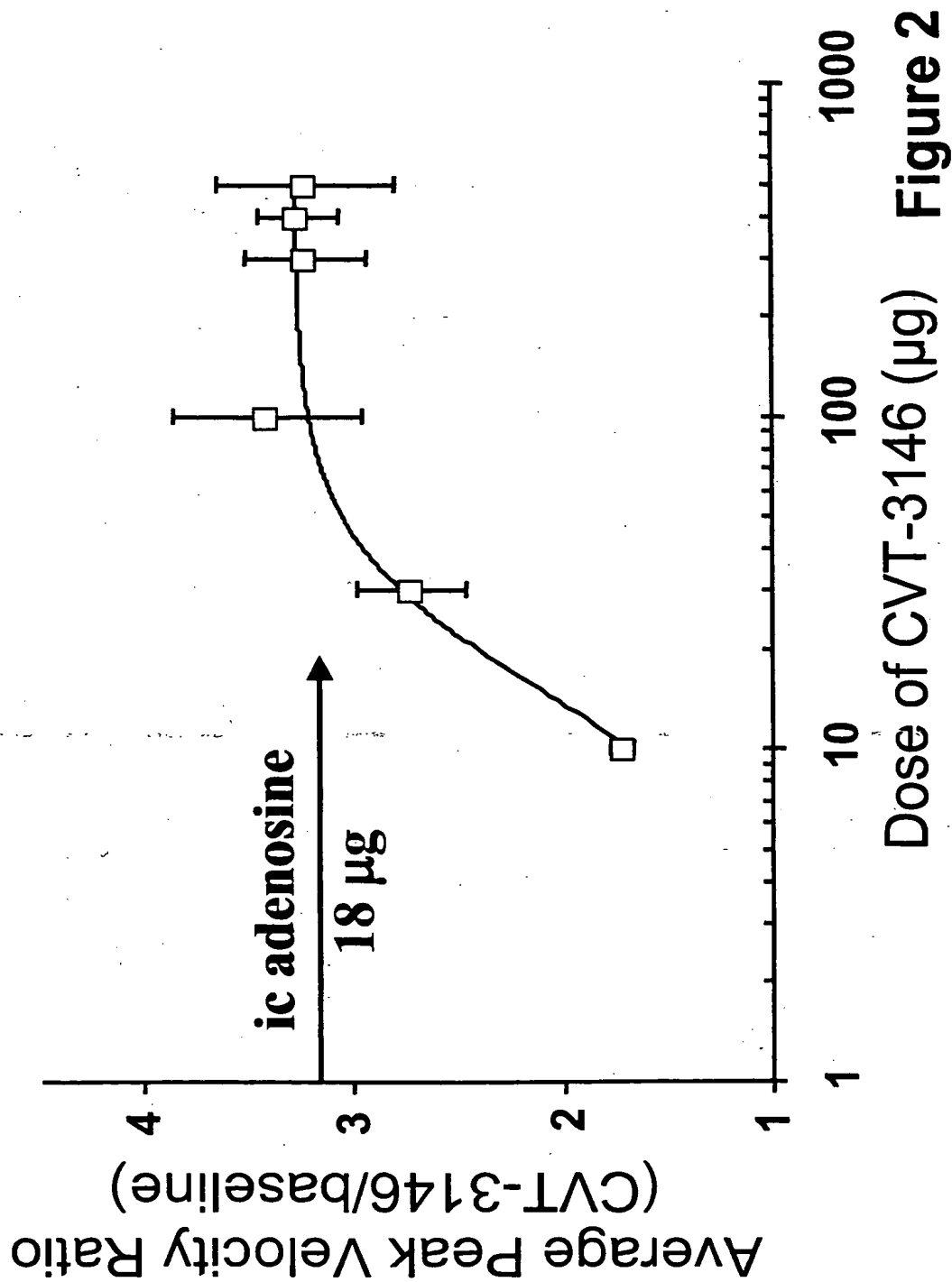
Adenosine 18 μ g
ic bolus



CVT-3146 30 μ g
iv bolus

Figure 1

Dose-Dependent Increase in Peak Flow Velocity Caused by CVT-3146



CVT-3146 and Coronary Flow Velocity

Duration of Effect:

Dose (n)	Duration ≥ 2.5 Baseline Mean \pm SEM
10 μg (4)	0
30 μg (4)	0
100 μg (3)	0.2 \pm 0.2 minutes
300 μg (4)	2.2 \pm 1.3 minutes
400 μg (8)	2.8 \pm 0.8 minutes
500 μg (4)	2.9 \pm 1.3 minutes

3/17

Figure 3

Time Course of APV Ratio (CVT-3146 400 μ g)

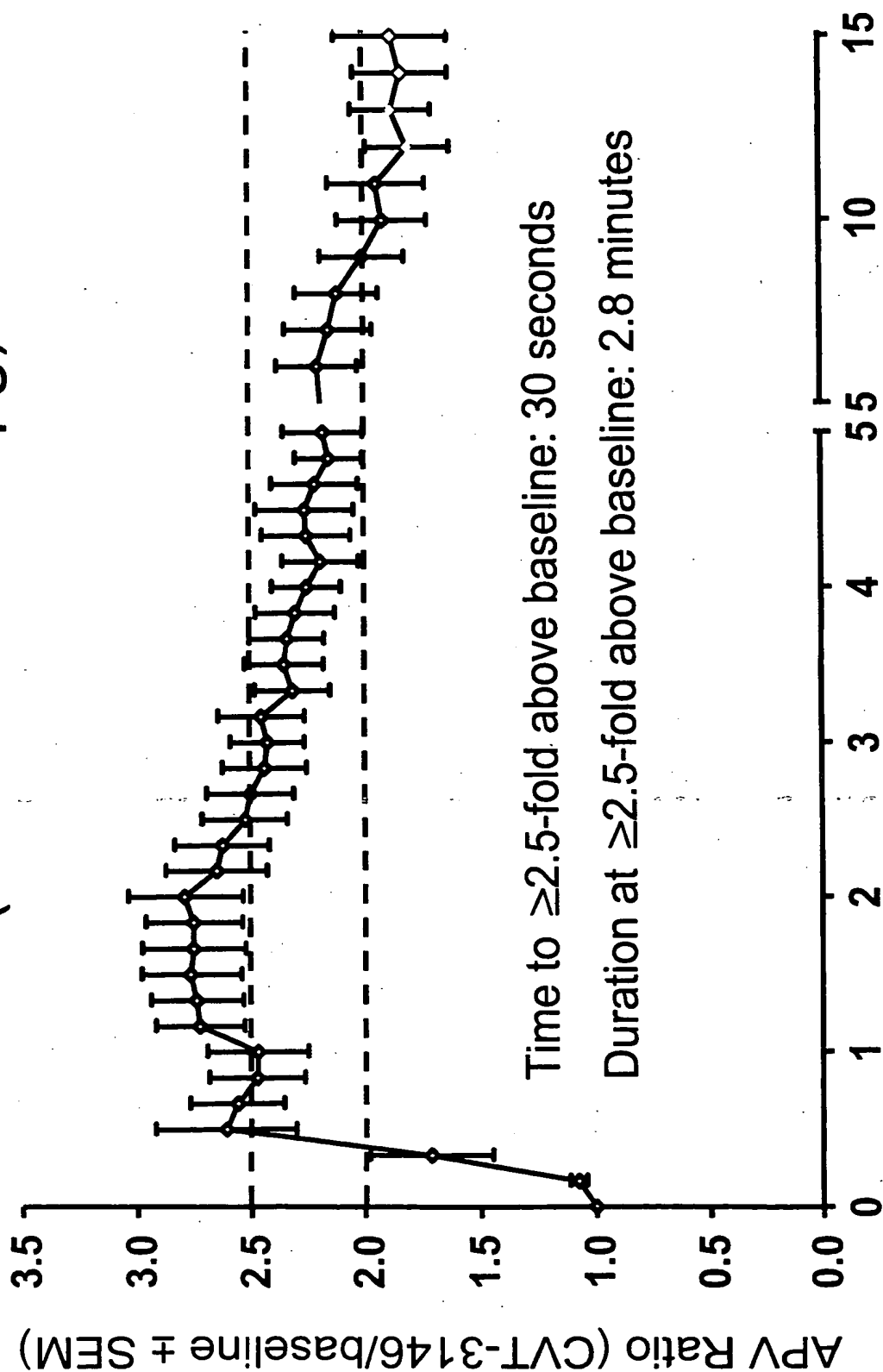
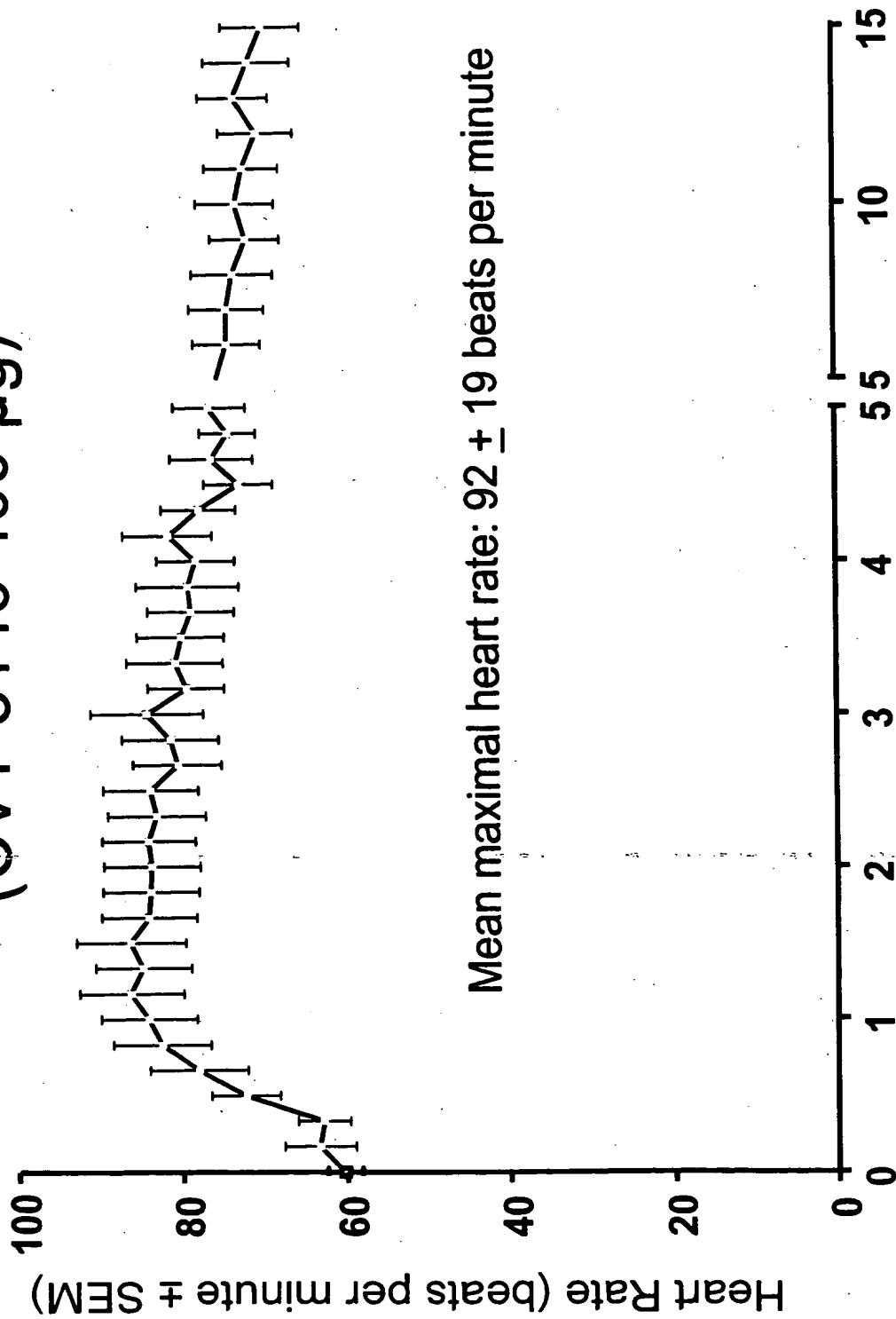
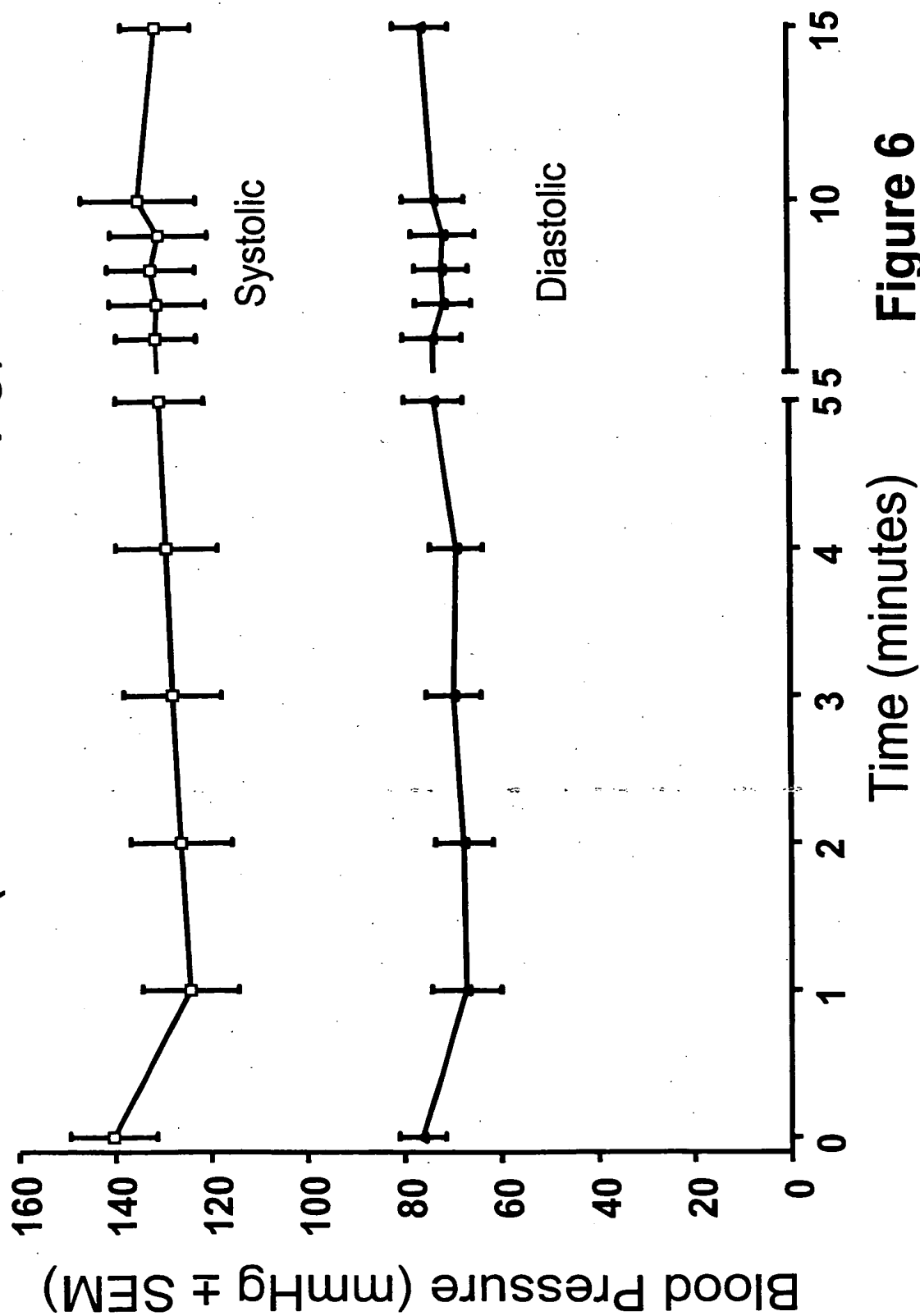


Figure 4

Time Course of Heart Rate (CVT-3146 400 µg)



Time Course of Blood Pressure (CVT-3146 400 μ g)



All Drug-Related Adverse Events Were Mild and Transient

Adverse Event	All Doses	
	(n = 36)	400 µg (n = 9)
chest discomfort	3	3
increased heart rate	3	1
hypotension	2	2
flushing	2	1
shortness of breath	2	0
funny taste in mouth	1	0
sensation in mouth, sinus, and chest	1	0
headache	1	0
tingling in hands	1	1
heart racing	1	1
bradycardia	1	1
lightheadedness	1	1
cough	1	0
nausea and vomiting	1	0

7/17

Figure 7

Figure 8

Mean CVT-3146 Plasma Concentration in Healthy Male Volunteers - Supine Position

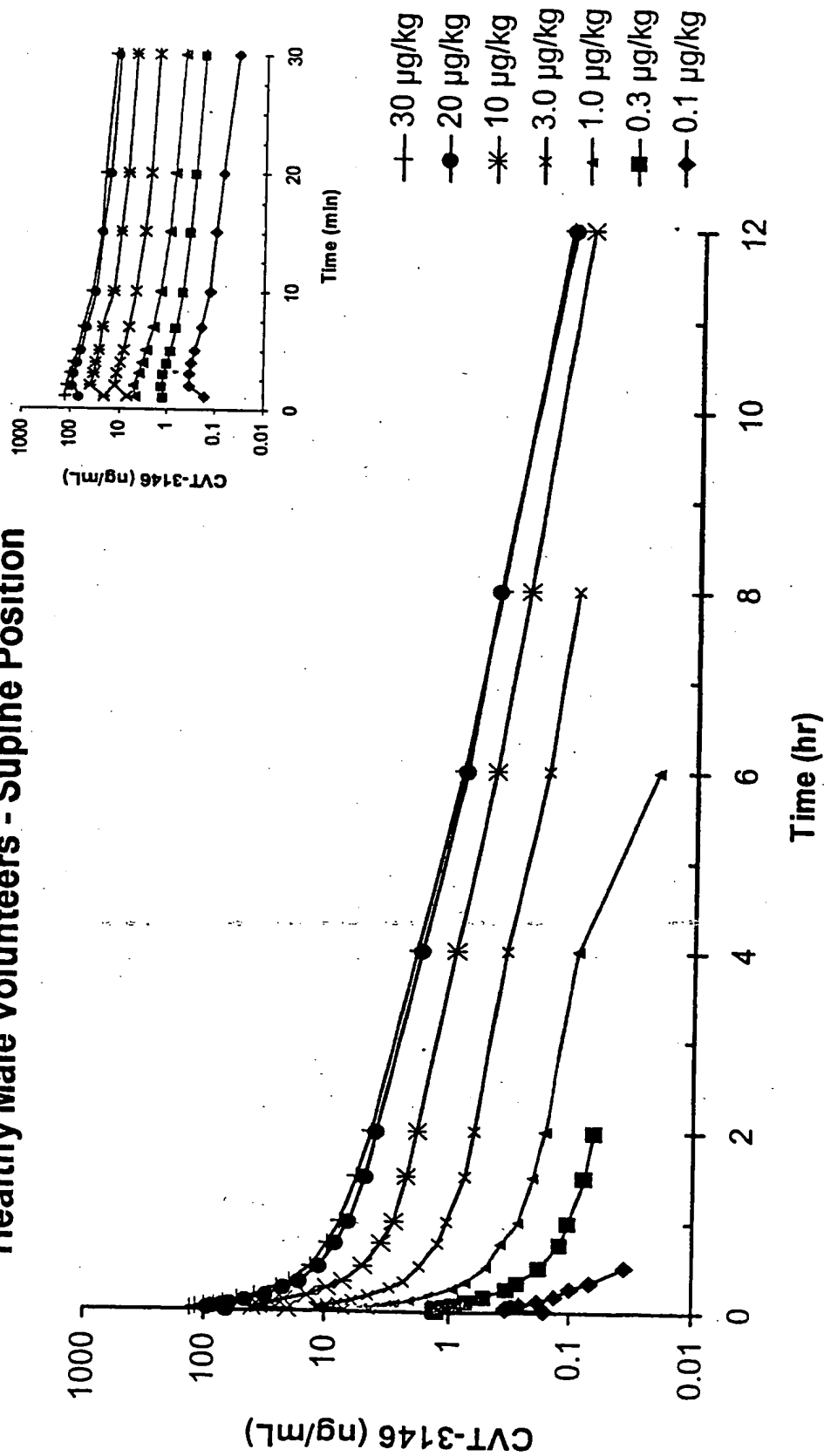


Figure 9

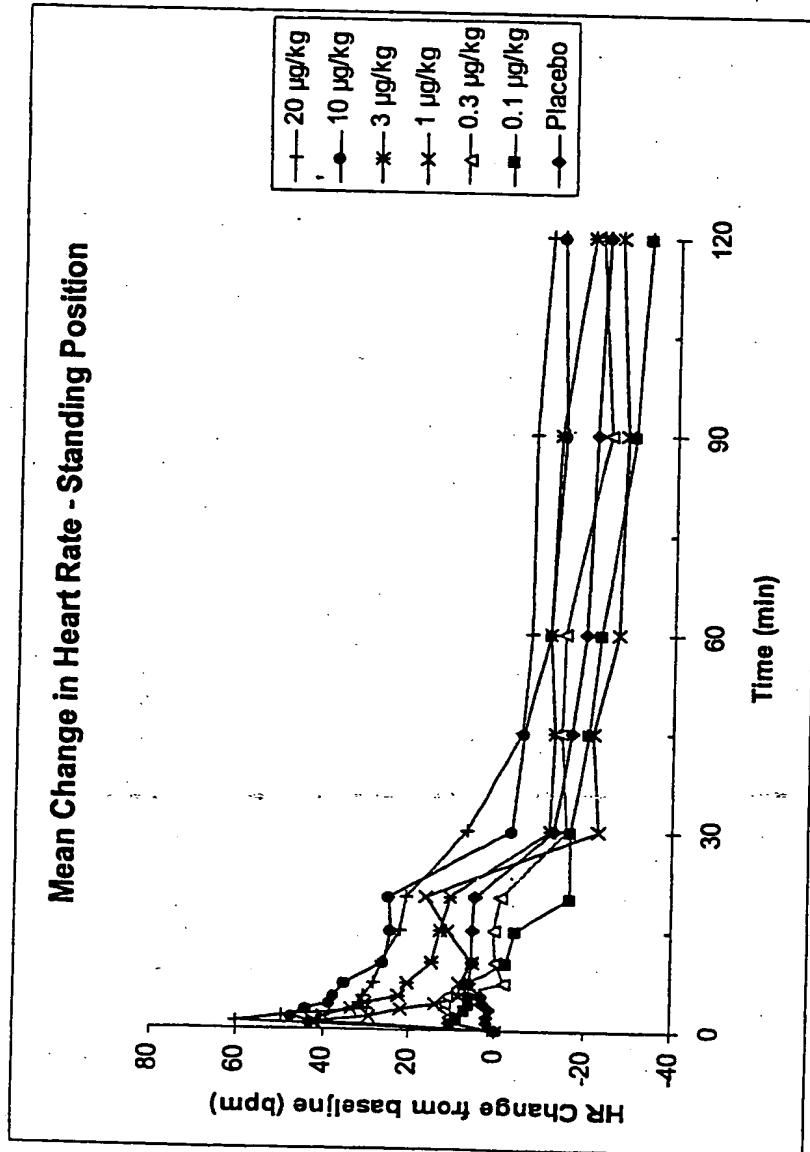


Figure 10

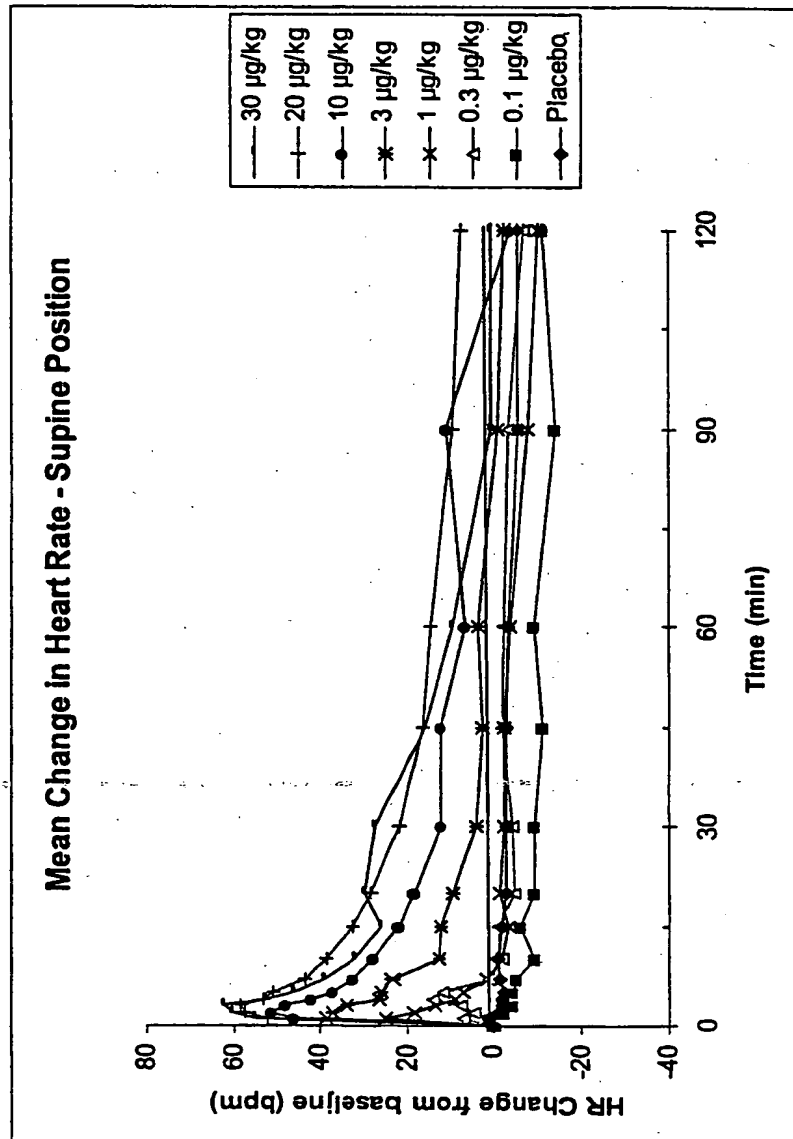


Figure 11

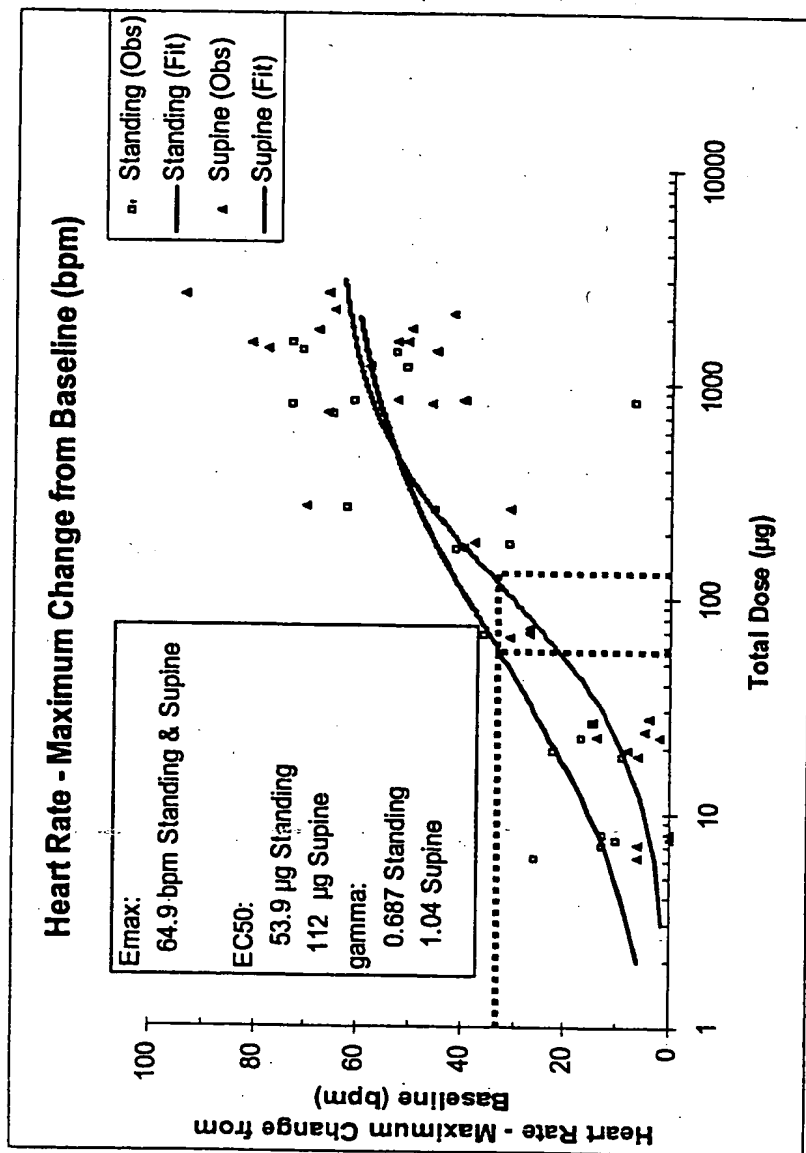


Figure 12

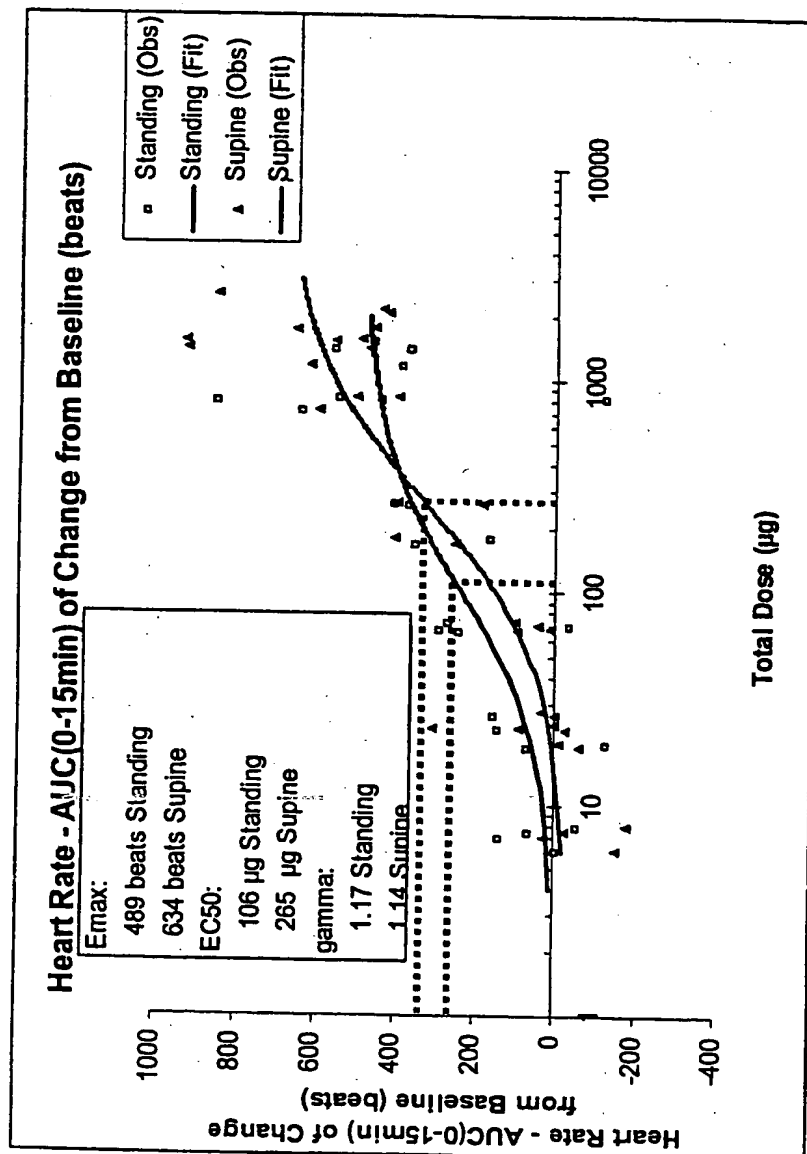


Figure 13

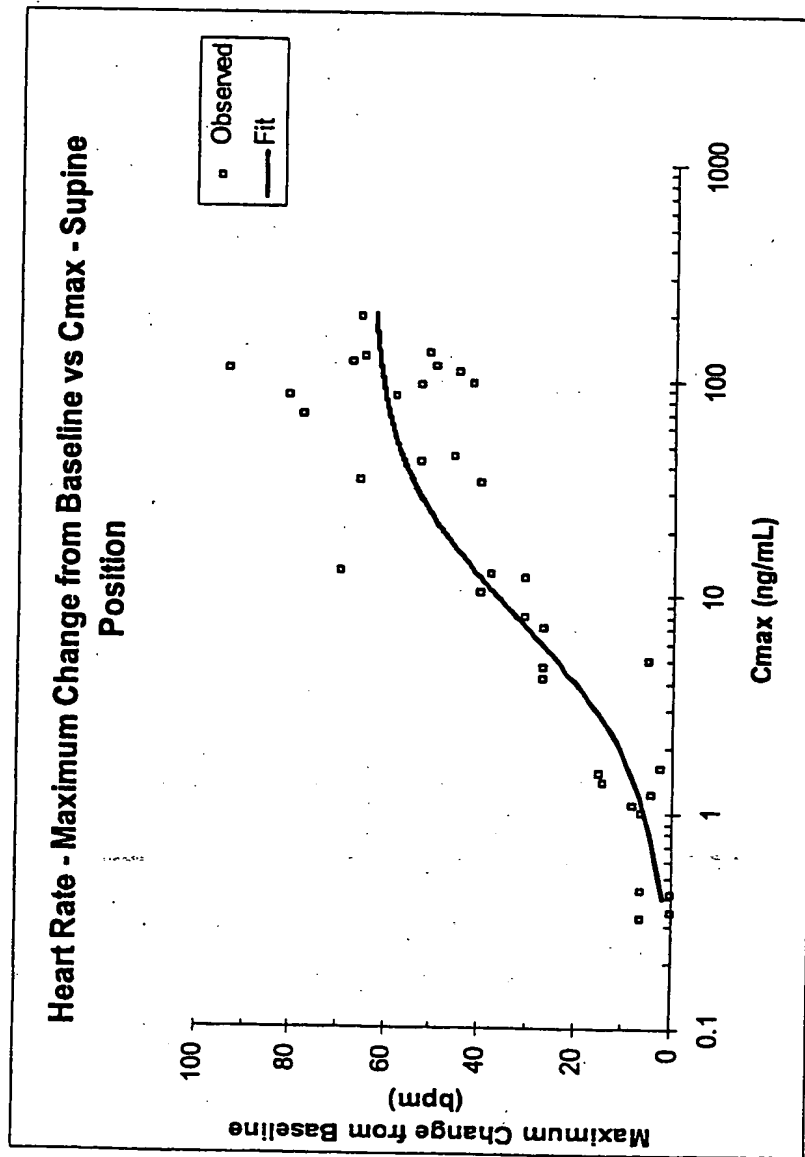


Figure 14

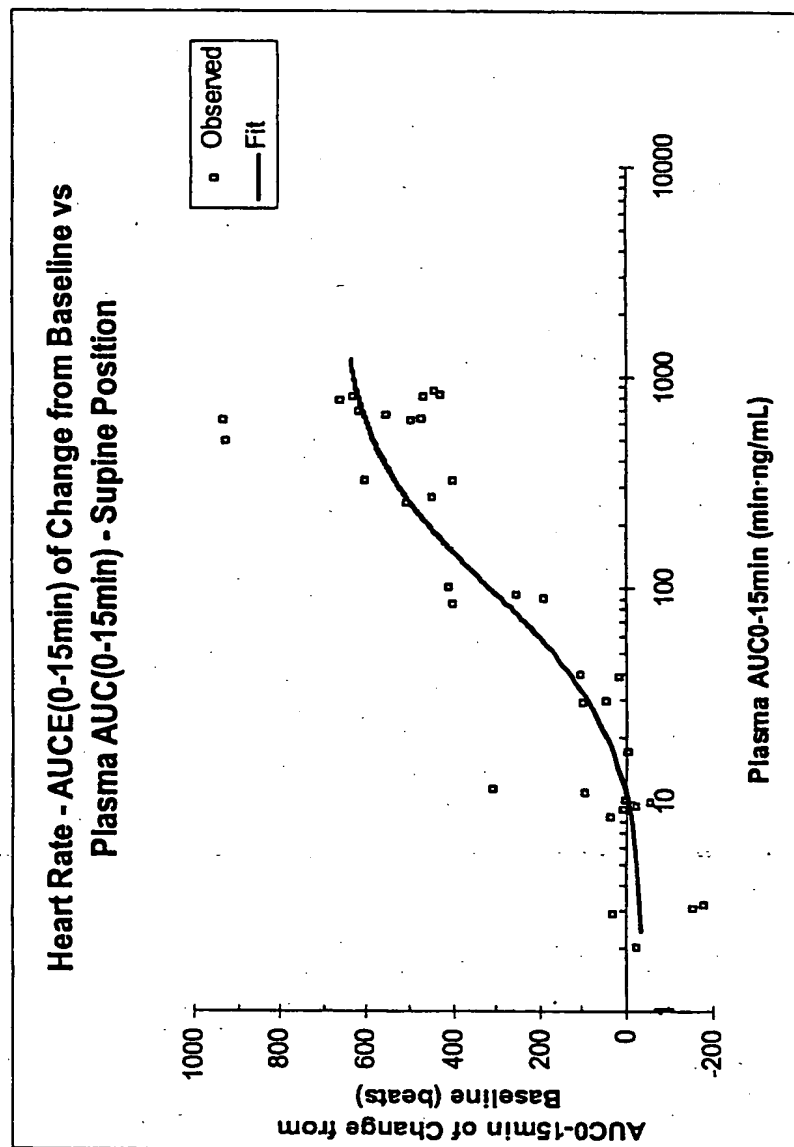
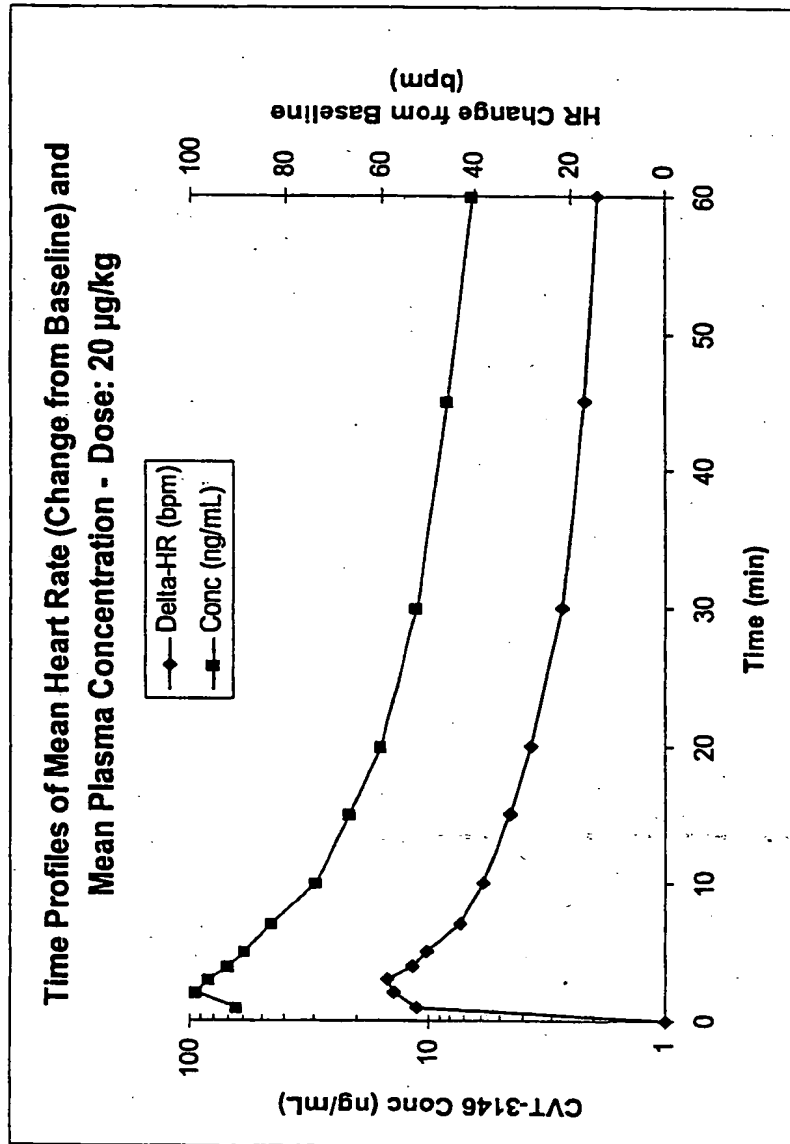
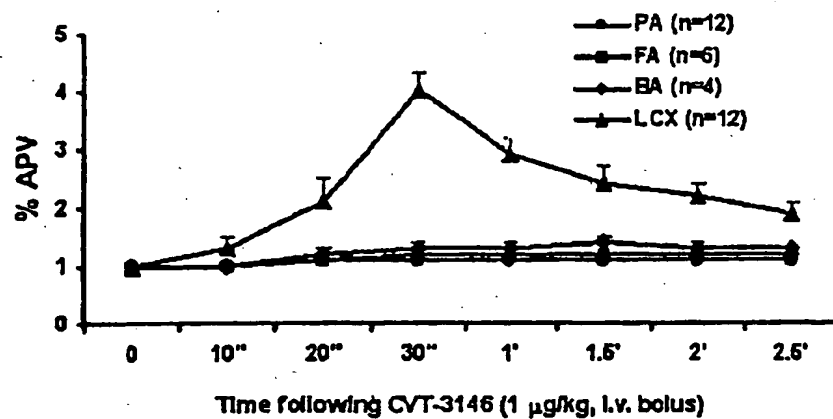
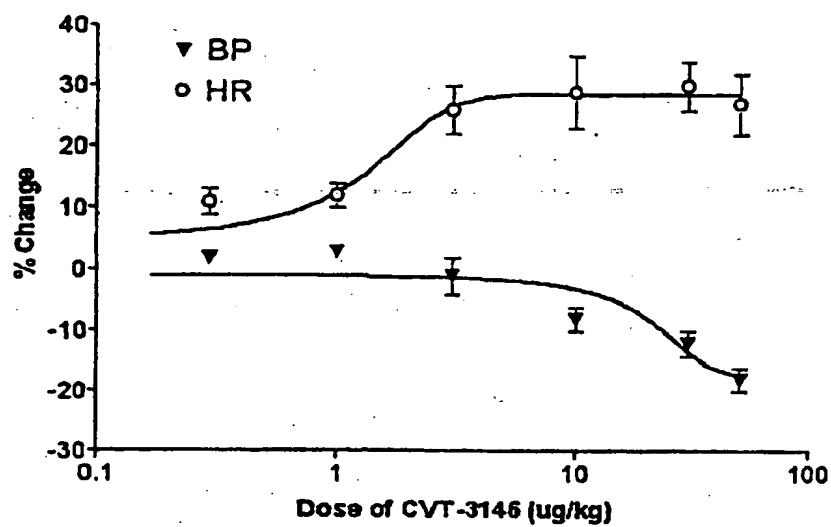


Figure 15



**Figure 16****Figure 17**

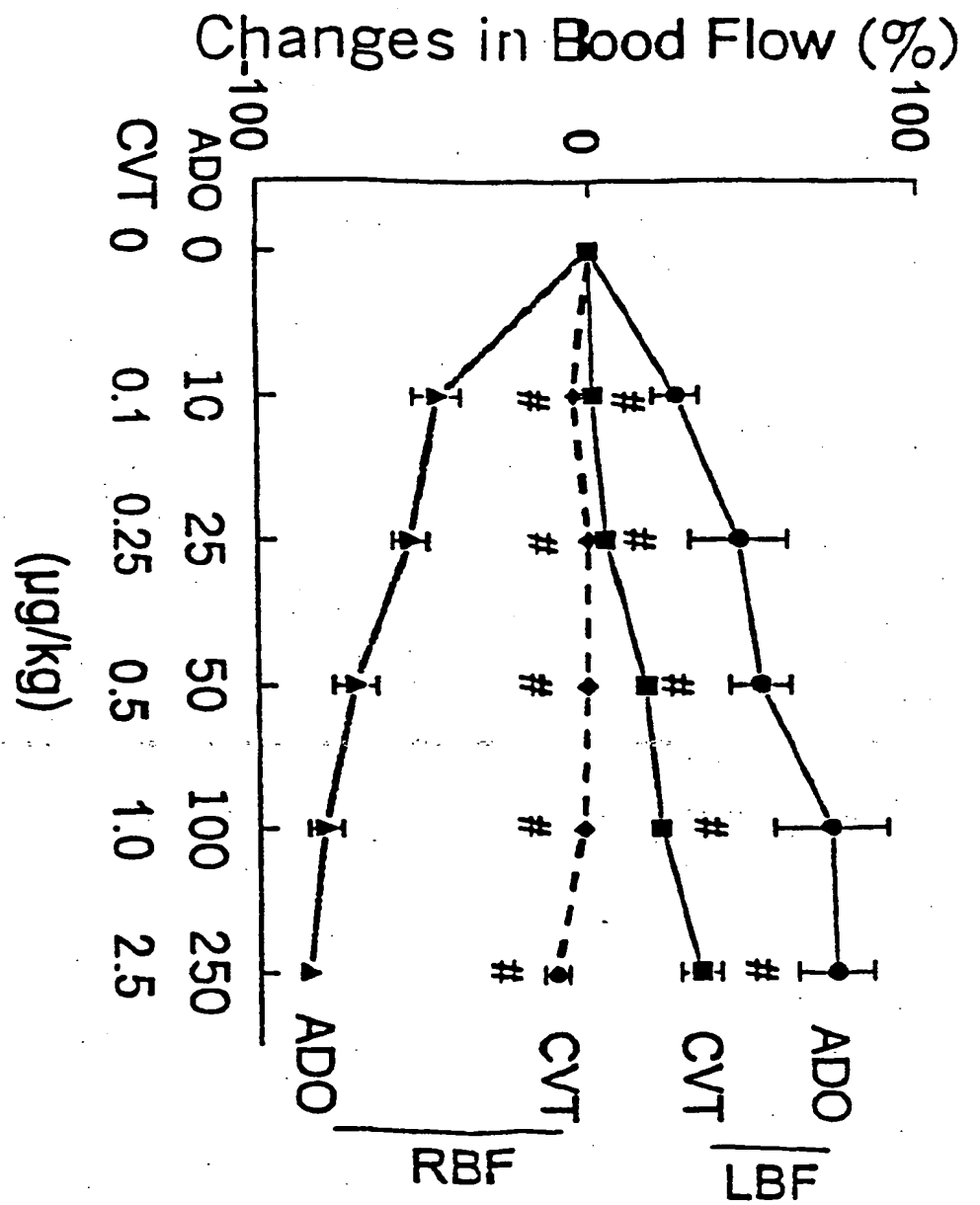


Figure 18